REMARKS

Claims 46-52, 54, 58-59 and 61-70 are pending in the present application. Claims 54, 61 and 62 have been withdrawn by the Examiner as being drawn to a nonelected species.

Applicants respectfully request that the remarks made herein be entered and fully considered.

The Rejections Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 46, 49-52, 58, 59 and 63-70 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over by U.S. Patent No. 6,146,632 (the " '632 patent") in view of U.S. Patent No. 4,727,064 (the " '064 patent") for the reasons of record. Applicants respectfully disagree for the reasons set forth in the Amendment Under 37 C.F.R. § 1.116 filed on October 13, 2006 and for the additional reasons discussed below.

First, Applicants respectfully submit that the Examiner has not provided a convincing line of reasoning as to why the present invention is obvious over the cited references[1].

> The initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985).

See MPEP § 2142.

The '632 patent describes the use of oil in water emulsions in combination with QS21 to enhance immune responses to a given antigen. See '632 patent, col. 1, lines 28-34. As noted by the Examiner, the '632 patent does not teach a beta-cyclodextrin.

The Examiner contends that the '064 patent teaches that hydroxypropyl-beta-cyclodextrin (HPCD) improves solubility (which reduces the tendency to cause irritation), and that HPCD stabilizes a wide range of drugs (including steroid), exhibits low toxicity, extends shelf life and is widely used as an excipient.

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[1] Neither the '632 patent nor the '064 patent expressly or impliedly suggests the combination of (1) a *Quillaja saponaria* saponin adjuvant and (2) a β-cyclodextrin or deacylsaponin.

The Examiner concludes that it would have been obvious to employ HPCD as an excipient, as taught by the '064 patent, in an immunogenic composition comprising QS21 and antigen, as taught the the '632 patent. This conclusion is premised on the Examiner's contention that a person of skill in the art would have been motivated to do so because the '064 patent teaches that HPCD adds stability to any drug and extends shelf life, reduces irritation and exhibits low toxicity.

Applicants respectfully submit that the Examiner's characterization of the teachings of the '064 patent is incorrect. The '064 patent teaches that water-soluble cyclodextrins improve the solubility of crystalline drugs with low solubility. See the '064 patent, col. 1, lines 26-36. There is no teaching or suggestion in the '064 patent that HPCD can be used with anything except drugs with substantially low water solubility that tend to crystallize.

There is no teaching or suggestion in either the '064 patent or the '632 patent that antigens or saponin adjuvants tend to crystallize and have poor water solubility, or that such is a concern in immunization procedures. Therefore, Applicants respectfully submit that the Examiner has not provided a convincing line of reasoning to combine the '064 patent, which teaches the use of cyclodextrin mixtures to improve the solubility of crystalline drugs with substantially low water-solubility, with the '632 patent, which teaches vaccine formulations that are oil-in-water emulsions in combination with QS21 to enhance immune responses to a given antigen. Thus, the '632 patent in view of the '064 patent does not render the invention *prima facie* obvious.

Second, Applicants respectfully submit that the Examiner has not shown in the Advisory Action that Applicants' evidence of unexpected results was considered by the Examiner.

> When an applicant submits evidence, whether in the specification as originally filed or in reply to a rejection, the examiner must reconsider the patentability of the claimed invention. The decision on patentability must be made based upon consideration of all the evidence, including the evidence submitted by the examiner and the evidence submitted by the applicant. A decision to make or maintain a rejection in the face of all the evidence must show that it was based on the totality of the evidence. Facts established by rebuttal evidence must be evaluated along with the facts on which the conclusion of obviousness was reached, not against the conclusion itself. *In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990).

See MPEP § 2142 (emphasis added).

The Examiner's conclusory statements that Applicant's arguments were fully considered but were not persuasive does not show that it was based on the totality of the evidence. The Examiner has provided no reasons why Applicants' unexpected results are not persuasive in showing the nonobviousness of the claimed invention. Applicants respectfully request that the rejection be withdrawn or that the Examiner provide reasons for her conclusions so that Applicants can address such reasons.

Claims 46-52, 58, 59 and 63-70 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over the U.S. Patent No. 5,057,540 (the "'540 patent") in view of the '064 patent for the reasons of record. Applicants respectfully disagree for the reasons set forth in the Amendment Under 37 C.F.R. § 1.116 filed on October 13, 2006 and for the additional reasons discussed below.

First, Applicants respectfully submit that the Examiner has not provided a convincing line of reasoning as to why the present invention is obvious over the cited references.

The '540 patent describes the use of immunologic compositions comprising a saponin adjuvant in combination with an antigen component. As noted by the Examiner, the '540 patent does not teach a beta-cyclodextrin.

The Examiner contends that the '064 patent teaches that hydroxypropyl-beta-cyclodextrin (HPCD) improves solubility (which reduces the tendency to cause irritation), and that HPCD stabilizes a wide range of drugs (including steroid), exhibits low toxicity, extends shelf life and is widely used as an excipient.

The Examiner concludes that it would have been obvious to employ HPCD as an excipient, as taught by the '064 patent, in an immunogenic composition comprising QS21 and antigen, as taught by the '540 patent. This conclusion is premised on the Examiner's contention that a person of skill in the art would have been motivated to do so because the '064 patent teaches that HPCD adds stability to any drug and extends shelf life, reduces irritation and exhibits low toxicity.

As discussed above, Applicants respectfully submit that the Examiner's characterization of the teachings of the '064 patent is incorrect. The '064 patent teaches that water-soluble cyclodextrins improve the solubility of crystalline drugs with low solubility. See the '064 patent, col. 1, lines 26-36. There is no teaching or suggestion in the '064 patent that HPCD can be used with anything except drugs with substantially low water solubility that tend to crystallize.

There is no teaching or suggestion in either the '540 patent or the '064 patent that antigens or saponin adjuvants tend to crystallize and have poor water solubility, or that such is a concern in immunization procedures. Therefore, Applicants respectfully submit that the Examiner has not provided a convincing line of reasoning to combine the '064 patent, which teaches the use of cyclodextrin mixtures to improve the solubility of crystalline drugs with substantially low water-solubility, with the '540 patent, which teaches delivering an antigen to which an immune response is desired using a saponin adjuvant to enhance the immune response. Thus, the '540 patent in view of the '064 patent does not render the invention *prima facie* obvious.

Second, for the reasons above, Applicants respectfully submit that the § 103 rejection should be withdrawn, because the Examiner does not appear to have considered Applicants' evidence of unexpected results.

In view of the foregoing, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

Applicants respectfully request that the present remarks be made of record in the instant application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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